SOME OBSERVATIONS ON PRIMARY CARCINOMA OF THE LIVER, WITH REFERENCES TO MUSEUM SPECIMENS.

By

F. J. WHEELER, M.R.C.S., L.R.C.P.

(From the Pathological Department.)

An examination of the post-mortem records of Guy's Hospital for ten years (1897–1906 inclusive) gave an apparent total of 15 cases of primary carcinoma of the liver out of 5,233 autopsies. On further investigation these could be divided up as follows:—

(a.) Where growth was present in *more than one* other organ:—

1. P.M. 389, 1902. In heart and kidney.
2. P.M. 440, 1903. Carcinomatous infiltration of cervical glands, pleura, spleen, and kidneys.
3. P.M. 144, 1904. Involvement of stomach, omentum, peritoneum, lungs and pleura. (Specimen 04/23. Curator's Room.)
4. P.M. 531, 1904. Glands in right iliac fossa, and a mass surrounding cæcum. Mass in prostate (said to be a fibro-adenoma).
5. P.M. 268, 1905. Growth in uterus, peritoneum, retro-peritoneal glands, pancreas and supraclavicular gland.

(b.) Where growth was present in *one* other organ, or glands only involved :—

1. P.M. 162, 1898. In right lung. (Specimen 98/29. Curator's Room.)
2. P.M. 246, 1902. Glands in portal fissure involved. (Specimen 02/25. Curator's Room.)
3. P.M. 523, 1902. Glands in portal fissure involved. (Specimen 02/47. Curator's Room.)
4. P.M. 251, 1903. Glands near pancreas involved. (Specimen 03/38. Curator's Room.)
5. P.M. 408, 1903. In fourth dorsal vertebra. (Dr. Nicholson's slides.)

(c.) Where no growth could be found elsewhere :—

1. P.M. 397, 1897. No specimen or slides available.
2. P.M. 64, 1897. " " "
3. P.M. 297, 1900. (Slide from post-mortem inspection.)
4. P.M. 61, 1905. (Specimen 05/11. Curator's Room.)
5. P.M. 527, 1905. (Dr. Nicholson's slide.)

In group (a) it seemed unlikely that any of these could be primary growths in the liver. A specimen of the liver from P.M. 144, 1904, was preserved in the museum. Microscopically the growth was secondary to growth elsewhere, probably breast. No material could be obtained of the remaining livers in this group, and they have, therefore, also been excluded.

In group (b) specimens or slides were available of all, and four out of the five were definitely primary carcinomata. The fifth case (P.M. 251, 1903) was secondary to growth elsewhere, in all probability prostate.

In group (c) two cases (P.M. 64 and P.M. 397, 1897) have been rejected, no slides or specimens being available. In another instance (P.M. 297, 1900), although no growth was found in any other organ, microscopically the growth in the liver is obviously not of hepatic origin. The two remaining cases are genuine instances of primary carcinoma.

The cases which are microscopically those of primary carcinoma are the following :—

1. P.M. 162, 1898. (Specimen 98/29. Curator's Room.)
2. P.M. 246, 1902. („ 02/25. „ „)
3. P.M. 523, 1902. („ 02/47. „ „)
4. P.M. 61, 1905. („ 05/11. „ „)
5. P.M. 527, 1905. (Dr. Nicholson's slides.)
6. P.M. 408, 1903. („ „)

It is obvious from the results obtained by the above analysis that a very careful microscopic examination is necessary before any case can be considered to be one of primary hepatic cancer. The apparent absence of growth elsewhere is no absolute guide. Growth may be latent in other organs and yet give rise to secondary deposits in the liver. This possibly is the explanation of the case in group (b.), P.M. 251, 1903, where the only other growth found was in glands near the head of the pancreas, and microscopically the liver tumour was of extraneous origin. Again in group (c.), P.M. 297, 1900, the only growth that could be found in this instance was in the liver, and microscopically it obviously had its origin elsewhere. Cases have been recorded where prostate has been normal to the naked eye, and yet microscopic examination was able to demonstrate the presence of malignant disease. The same is true of breasts and other glandular structures. The possibility of cancer having been present in an appendix removed during life should also be borne in mind.

During the same period (1897—1906) there were 144 instances of secondary cancerous deposits in the liver, the numerical ratio between primary and secondary hepatic cancer thus being 1 to 21 nearly. Secondary cancer is stated to be much more common in women than men, owing to the great frequency of uterine and mammary cancer in females. An analysis of the 144 cases does not confirm this statement, as seventy-seven of the cases occurred in men and sixty-seven in women. The uterus and ovaries contributed seven and the female mammary glands five cases. It is probable that the explanation of this difference is that very few of the patients with breast cancer and

cancer of the female pelvic organs die in hospital. It may be that secondary deposits in the liver from these organs are not so common as they are generally believed to be. Another suggestion is that malignant disease is increasing in men. Out of 100 cases of secondary deposits, collected from the post-mortem records of St. George's Hospital for ten years (1892—1902), sixty-six were males and thirty-four females.[1]

Age and sex.—Primary hepatic cancer can occur at any age, although the usual time for it to appear is between the ages of 40 and 60 years. It is more often found in males than females; four out of the six cases occurred in the former. The ages of these patients were sixty-two, sixty-five, sixty-seven and thirteen years. The remaining two were in females, whose ages were thirty-two and sixty-two respectively.

Although primarily a disease of adult life, it occasionally occurs in children. An interesting series of primary malignant growths of the liver in children under fifteen years of age was published in 1897.[3] There were twenty-nine cases collected from the literature. Eleven of these were carcinomata, the remainder being sarcomata. The ages ranged from eight weeks to fourteen years. Recently two cases occurring in infants of seven and nine months have been recorded.[4]

Clinical Characters.

The six cases present a few points of clinical interest:—

Onset and early symptoms.—The onset was usually insidious, and marked by increasing gastric disturbance in four of the cases, where there was a definite alcoholic history. The earliest symptoms here were nausea on waking in the morning, accompanied in one instance by actual vomiting. Loss of appetite and inability to take solid food quickly followed. In one instance the gastric trouble was preceded by an increasing dislike of fat. Hæmatemesis and epistaxis occurred early in one case. The remaining two cases (case 1 and case 6) are clinically of exceptional interest. In one, the boy of thirteen years, no symptoms were present beyond slight drowsiness and an enlarging abdomen. He was admitted into Addison Ward, under Dr. Taylor, in April,

1898. Fourteen days before admission he was apparently quite well, and attending school. He then complained of his trousers being tight. It was noticed that his abdomen was unduly large. He seemed quite well otherwise beyond a slight drowsiness. The swelling increased, and he was brought to the hospital. There was a total absence of pain or discomfort. His condition on admission was as follows:—The abdomen was enlarged, measuring 27½ inches in circumference at the umbilicus. The abdominal wall was not tense, but there was some tenderness to the right of the umbilicus. A huge mass could be felt, which appeared to be the liver, on the right side reaching to the level of the anterior superior spine of the ilium. The surface of this mass was smooth; a slight protuberance was evident near the umbilicus. There were distended veins over the whole abdominal region. The pulse was rapid, being 125 per minute.

Progress of the case.—April 1st. On admission, there was some vomiting. An exploring needle was used to see if there was any ascites, but only a few drops of blood were obtained. A diagnosis of "sarcoma of the liver; possibly hydatid," was made. On April 2nd, a broad band of pigmentation appeared on the left side, which increased, and on the following day extended partly over to the right side of the abdomen. Slight œdema of the abdominal wall was noticed. On April 4th, patient was sick again; the pigmentation was well marked now on the right side. The veins of the chest wall were greatly swollen. The mass was again explored with a trochar and cannula, and again only a few drops of blood obtained. Pain was noticed for the first time on the 21st April accompanied by dyspnœa. The physical signs in the chest were normal. The patient became very much jaundiced, and the pain became very severe, necessitating the administration of morphia. Death took place on the 25th April.

This case illustrates the extreme rapidity of the disease, and also death from an unusual cause.[5] At the post-mortem death was found to be due to hæmorrhage into the peritoneal cavity.

In the remaining case, that of a man of sixty-seven, the initial symptom complained of was pain between the scapulæ, followed

later by paraplegia. Throughout the illness there were no symptoms suggestive of hepatic disease, although the paraplegia was due to a secondary deposit in the vertebræ, arising from a primary growth in the liver.

Pain.—Pain was not a marked feature in the early stages of the disease. It was rather a feeling of uneasiness and discomfort below the costal margin than actual pain. Pain in all the cases became severe towards the end.

Jaundice.—Jaundice was present in five out of the six cases. In three instances it occurred early, but was never very marked. In the other three cases it was late in onset, and in one instance only occurred three days before death.

Ascites.—Ascites was present in four instances, and occurred in the cases with a definite alcoholic history. Paracentesis was necessary. The fluid drawn off was pale yellow or orange in colour, alkaline or neutral in reaction. The specific gravity varied from 1010–1016. Albumen, chlorides, and traces of urea were present.

Urine.—The urine in five cases was darker in colour than normal. The amount passed varied with the presence or absence of ascites. The specific gravity ranged from 1020–1035. The reaction was acid, and a large amount of urates was present. The excessive quantity of urates is said to be a marked feature in hepatic cancer. The amount of urea increased in the early stage of the disease, being as much as 4·5 %, while towards the end it only amounted to 1·5 % or less. Bile pigment was present where jaundice occurred. Albumen was only present once.

Fæces.—The fæces were normal in colour in four cases. In the remaining two instances they were described as light yellow in one and clay-coloured in the other.

Temperature and pulse.—In one case the temperature was normal, or a little above, throughout, rising on two occasions to 100°. In three instances it was subnormal. In another the temperature was normal, with three exceptions, when it rose to 102°, 104°, and 101°. In the remaining instance, periods of pyrexia and apyrexia were present. In this case a rigor occurred once.

Pyrexia may be present in uncomplicated malignant disease. Usually the rise of temperature is not great. In some instances a peculiar tendency towards alternations of periods of pyrexia and apyrexia has been observed.[6]

Pulse.—The pulse was rapid in four cases, in one of which it averaged 125 beats per minute. In three it averaged 104 beats per minute. In the remaining two instances it varied between 80 and 90 beats per minute.

Prognosis.—From the onset of the earliest symptom until death the average duration of the disease was three and a half months. One patient lasted eight months. She was a woman (case 4), admitted as cirrhosis, who improved considerably, went out, and remained at home for three weeks; came back, again went out, finally returning to die. In the boy the disease was fatal in five weeks from onset. In the remaining cases death ended the scene in $3\frac{1}{2}$, 3, $2\frac{1}{2}$, and $2\frac{1}{2}$ months respectively. Five weeks was generally the duration of the illness from the time these patients were bad enough to remain in bed.

Diagnosis.—Mellanby has recently made an interesting discovery which may prove of considerable value in diagnosing malignant disease of the liver. It is that patients suffering from *cancer* of the liver excrete a considerable amount of creatin, a substance which normally does not appear in the urine. In *cirrhosis* and *engorged livers* creatin is *not* excreted, but the normal amount of creatinin is diminished.[7]

Pathology and Morbid Anatomy.

Origin of the new growth.—Cancer arising primarily within the liver may spring from any one of the following sources:—

1. Liver cells.
2. Bile ducts.
3. Suprarenal tissue and possibly "rests" of other organs.

Primary cancer in the majority of cases takes origin from the liver cells. More rarely it originates from the cubical epithelium of the small or columnar epithelium of the larger intra-hepatic ducts. The growth tends to spread rapidly, invading and compressing the normal tissue which in places

remains as mere strands. Occasionally growth spreading in spaces formed by the atrophy and necrosis of normal cells appears to be encapsuled. This apparent capsule is formed of flattened liver cells. At the margins of the growth many atypical multinucleated cells can often be seen. Various interpretations have been given in explanation of this phenomenon, which in all probability represents the final stage of the disappearing liver cells. The continuity between the normal cells and those of the neoplasm can in many instances be made out by careful microscopic examination. The resemblance to liver cells is not always found in these primary growths, as occasionally a reversion to the embryonic type of cells takes place. In other cases growth arises from tissue of other organs, such as pancreas or suprarenal, included in the liver. It has been stated to be not uncommon to find suprarenal tissue. In the kidney the somewhat familiar "adrenal rest" tumour is sometimes found, and one case is on record where a similar "rest" in the liver gave rise to malignant disease. Primary carcinoma from the intra-hepatic bile ducts is extremely rare.

The relation of cirrhosis to cancer.—The question of cancer arising in a cirrhotic liver is an extremely interesting one. Three theories have been held at various times :—

1. That cirrhosis and cancer both develop together.
2. That cancer is the primary change.
3. That cirrhosis develops first.[1]

The last is the generally accepted theory, and recent work tends to show that cirrhosis is indirectly responsible for the malignant change in the liver cells. Experimentally it has been demonstrated that excision of a large portion of the liver in animals is followed by more or less complete renewal within a short period. The same phenomenon has been observed, but to a lesser extent, in man. A very good example was found in the case of a man whose liver had been lacerated in an accident.[8] He died, seventeen days after the injury, from empyema. At the post-mortem blood-clot was seen filling up the spaces caused by the injury. Microscopically it was shown that at the margins, and running into the blood-clot, there were columns of new liver cells,

together with connective tissue elements. In the one case the process is a simple compensatory hypertrophy, while in the other it is a direct attempt at repair by means of connective tissue and *proliferation* of cells. This power of regeneration by the liver cells is present at all ages, though naturally the younger the individual the more likely it is to take place. If this proliferation of cells continues beyond a certain point it becomes abnormal, and the starting place of malignancy. In certain morbid conditions of the liver, *e.g.*, cirrhosis, acute yellow atrophy, and atrophy resulting from venous back pressure, atypical masses of cells occur. These represent efforts on the part of the liver to repair and replace damaged tissue. These areas of atypical parenchyma have been termed "regeneration nodules."[9] The cells do not form columns radiating from a central vein, but are arranged in a somewhat concentric manner. The intra-lobular and portal veins are few. From this stage the "regeneration nodules" go on to that known as "regeneration adenomata." The cells here are smaller; their growth is rapid, producing pressure effects on the surrounding tissue. There is very little trabecular arrangement, and very few capillary spaces. This stage merges into that of the "malignant adenoma," which consists of broad masses of cells lying in lymphatic and vascular spaces. These cells are arranged in columns separated by capillaries, and, finally, invade the liver in all directions.

The earlier changes can be seen in a large number of cirrhotic livers. The question then arises, why is it, since cirrhosis is so frequently met with, there are so few cases of cancer arising from this source? The answer most probably is that these atypical cell-masses become strangled and atrophy in the majority of these diseased livers. Microscope slides from case 3 show very clearly the changes immediately preceding carcinoma in a cirrhotic liver. In one slide "regeneration nodules" and "regeneration adenomata" are present, but there is no evidence of malignancy. Other slides from the same case show quite well the presence of new growth invading the vessels and producing compression effects. In almost every case of hepatic carcinoma, whether primary or secondary, the portal and hepatic veins

become filled with malignant thrombi. Thrombosis of these veins is a feature which does not appear to be generally recognized. Closely connected with the presence of malignant thrombi in the veins is the question of metastases. Secondary deposits from primary hepatic carcinoma do occur, but perhaps less frequently than from cancer elsewhere. They are carried by the blood stream, rarely by the lymphatics, and are found principally in lungs and pleura, and occasionally in bones (case 6).

Case 1.—Primary carcinoma. (Curator's Room, Specimen 98/29. Inspection 162, 1898.)

H. R., æt. 13. Schoolboy. Admitted April 1st, 1898, under the care of Dr. Taylor. Died April 25th, 1898.

Clinical history.—This has been given above.

Summary of the autopsy, which was performed by Sir Cooper Perry.—The body was wasted ; the skin was jaundiced, of a light yellow colour. The lung bases were compressed. Petechial hæmorrhages were present beneath both layers of the pericardium. The heart was normal. There were adhesions between the intestines. A considerable quantity of blood of recent date was found in the peritoneal cavity. The testes and pelvic organs were not examined. The glands in the portal fissure were enlarged.

Liver, 163 ozs.—The anterior surface was adherent to the abdominal wall. The whole organ was enormously and uniformly enlarged. It was full of masses of bile-stained growth, the central parts of which showed caseation, while at the periphery of them some hæmorrhage was present. There was very little healthy tissue left. The origin of the growth was thought to be probably in the thicker part of the liver. The liver edge in parts was approximately normal.

Secondary deposits.—One small deposit of growth was found on the surface of the upper part of lower lobe of right lung.

Description of museum specimen.—A slice right through the liver, showing many large lobulated white nodules of new growth. Into many of these hæmorrhage has occurred. Between the large lobules there are some scattered nodules, varying in size from mere specks to a pin's point. The branches of the hepatic

vein present numerous nodules of new growth projecting into their lumen. Some branches are distended and blocked with new growth. In places the liver has a "nutmeg" appearance, and especially in the large nodules.

Histology.—Examination of slides shows:—

1. Growth invading normal tissue, causing compression and atrophy of liver cells, which in many places remain as mere strands with flattened nuclei.

2. Masses of large atypical multi-nucleated cells in the compression areas and bordering on the new growth, representing possibly attempts at regeneration on the part of the disappearing normal tissue.

3. The new growth is composed of cells having little resemblance to liver cells, and is advancing along spaces apparently formed by necrosis and atrophy of liver tissue. It is arranged in irregular columns, with spaces in them containing bile. The presence of bile is constant throughout the growth, and is suggestive of the hepatic origin of the neoplasm.

4. The growth resembles suprarenal tissue, but the presence of bile in it, and the continuity between its cells and those of the liver, which can be traced here and there, almost certainly prove its hepatic origin. It is probably a reversion to the embryonic type of liver cell.

5. The growth is breaking down in places, and hæmorrhage into it has occurred, with destruction of its cells.

Case 2.—Cirrhosis and primary carcinoma. (Curator's Room, specimen 02/25. Inspection 246, 1902.)

Clinical history.—A. E., æt. 62, male. Admitted 25th May, 1902, under the care of Dr. Newton Pitt. Died 10th June, 1902. He came in for swelling of the abdomen and œdema of the legs. He had suffered from "bilious attacks" for years. There was a definite alcoholic history. There was a history of illness for three months before admission; swelling of abdomen, slight jaundice and pain. After admission, bleeding from nose and gums occurred, and ascites increased. Paracentesis was performed. The patient gradually became weaker and died.

Summary of the autopsy, which was performed by Dr. Bryant.—The body was wasted, and markedly jaundiced. The legs were œdematous. Heart: The endocardium was deeply stained with bile, and the intima of the vessels was also bile-stained. Fluid was present in the peritoneal cavity.

Liver, 4,210 grammes.—This organ was very much enlarged, and the surface was irregular and nodular. The nodules were not very large. The whole liver was involved, and many small nodules projected from the surface. These were deep, almost olive-green in colour, and were soft and fluctuating. The superficial blood-vessels were dilated. The tissue between the nodules was pinkish-grey in colour. A large mass of yellowish growth, nearly the size of a billiard ball, was present on the under surface of the liver. It was situated about five cm. above the neck of the gall-bladder and extended into it. No growth could be found elsewhere in the body.

Description of museum specimen.—A portion of the liver of brownish appearance, in which there is a certain amount of cirrhosis between the lobules. The latter stand out well. The liver is studded all over with small green bile-stained nodules, the larger of which are necrotic in their centres. They average about ·5 cm. in diameter. Other larger and isolated nodules, whitish in colour, averaging 1·5 cm., can be seen. There is a small white nodule, apparently of new growth, projecting into a branch of the hepatic vein.

Histology:—

1. Considerable cirrhotic change in liver.
2. Masses of atypical cells showing clearly all the stages, from a "regeneration nodule" to a "malignant adenoma."
3. The continuity between the new growth and the liver cells can be made out.
4. Bile is present in the neoplasm.
5. The cells of the growth in places are arranged round spaces, and have the appearance of pancreas.

The slides from this case are particularly interesting in that they show how a primary carcinoma of the liver may simulate

other tissues. Thus, while an examination of one microscope slide shows a resemblance to pancreas, an examination of others proves it to be definitely of liver origin.

Case 3.—Cirrhosis and primary carcinoma. (Curator's Room, Specimen 02/47. Inspection 523, 1902.)

Clinical history.—W. J., æt. 65. Stoker in brewery. Admitted 23rd October, 1902, under the care of Dr. Bryant. Died November 24th, 1902. He was admitted for ascites, and gave a definite alcoholic history. The first symptoms were noticed two months before his admission, and were those of early morning nausea and increasing size of abdomen. After admission the ascites increased and paracentesis was performed. The patient gradually became worse; vomiting and hæmatemesis occurred. He became slightly jaundiced towards the end, which rapidly followed on drowsiness and coma.

Summary of the autopsy, which was performed by Dr. Bryant.—The body was very emaciated. The skin was sallow and slightly jaundiced. Slight brown pigmentation of the face was noticeable. The veins at the lower end of the œsophagus were dilated.

Liver 2310 *grms.*—This organ was pale yellow in colour. Its surface was irregular and nodular, the nodules being small. In places projecting from the surface were a number of brownish-green soft nodules, some being about 2 cm. in diameter. The liver substance was harder than normal. Its edge was thick and irregular. On section, the organ was pale and apparently infiltrated with bands of fibrous tissue. There were streaks and patches due to fatty change.

Secondary deposits.—None. The glands in the portal fissure were enlarged. Sections were not cut of these. No growth could be found elsewhere.

Description of the museum specimen.—A sagittal section through the liver at its hilum. The upper half appears free from growth except for a few scattered white nodules in hepatic veins. Lobulation of this part of the organ is well marked, and to the naked eye shows no increase of fibrous tissue. The lower half of the liver is more fibrous and pale in appearance. It is almost entirely occupied by irregularly lobulated nodules of

new growth of varying size, from a pin's head to 2 cm. in diameter. The nodules are white or stained green with bile. The large branches of the hepatic vein at the hilum are entirely occupied and distended with white masses of new growth having hæmorrhage into them.

Histology.—

1. There is well-marked cirrhotic change in the liver, and the slides show extremely well "regeneration nodules" and "adenomata."

2. Typical glandular carcinoma arising from liver cells.

3. Section showing a vessel the walls of which are very much thickened. It contains within its lumen new growth.

Case 4.—Cirrhosis and primary carcinoma. (Curator's Room, Specimen 05/11. Inspection 61, 1905.)

Clinical history.—E. M., æt. 32. Female. First admission, August 4th, 1904. Last admission, December 2nd, 1904. Death, February 6th, 1905. She was said to have been quite well until June, 1904, when she had an attack of hæmatemesis, followed by diarrhœa and vomiting. She recovered and remained well until August, when she again had attacks of vomiting. On August 4th she was admitted, under the care of Dr. Pitt, for hæmatemesis. She had slight jaundice then, but no ascites. She left the hospital on October 3rd, to be readmitted again three weeks later, under the care of Sir Cooper Perry. This time she had well-marked ascites. She went out again on November 4th, to be readmitted on December 2nd, under the care of Dr. Pitt. Ascites was then very marked, and paracentesis was performed on three occasions, fifty-four pints of fluid being removed in all. Severe diarrhœa set in, followed by coma two days before death, which occurred on February 6th, 1905. (This history is unusually long for primary carcinoma, and suggests that the case, when first seen, was purely cirrhosis.)

Summary of autopsy, performed by Dr. Fawcett.—There was recent pleurisy over the right lung. The peritoneal cavity, which contained twenty pints of fluid, showed signs of recent peritonitis. The spleen, which was very large, weighed 620 grms.

Liver (weight not recorded).—This organ was much altered from the normal. In parts it showed well-marked cirrhosis, while other areas were occupied by deposits of soft growth stained a greenish-yellow colour with bile. The gall-bladder was normal.

Secondary deposits.—None.

Description of museum specimen.—A pale cirrhotic liver with a finely granular external surface. Some old adhesions and thickening of capsule can be seen. The cut surface is distinctly fibrous, and the liver lobulation exceedingly well-marked. This marking becomes more and more uniform near the upper part of the liver, so that the lobules merge into masses of new growth, between which are the fibrous bands. The upper part of the liver is entirely occupied by a mass of growth, necrotic in the centre. Some veins can be seen which are distended with new growth. The gall-bladder is slit open, and apparently is quite normal.

Histology.—Here again sections show "regeneration nodules and adenomata" in a cirrhotic liver, leading to typical hepatic carcinoma.

Case 5.—Cirrhosis and primary carcinoma. (Dr. Nicholson's slides. Inspection 527, 1905.)

Clinical history.—E. F., æt. 62, Female. Admitted 11th October, 1905, under the care of Dr. Taylor. Died 29th October, 1905. She was admitted for swelling of the abdomen. She had a definite alcoholic history. There was a six weeks' history of illness before coming to the hospital. This illness began with loss of appetite followed by pain, vomiting, and enlarging abdomen. There was no bleeding from nose or gums. On admission patient was jaundiced, and had well-marked ascites. Paracentesis was performed. Patient became gradually weaker and died.

Summary of autopsy, performed by Dr. Bell-Walker.—The body was wasted and slightly jaundiced. The lung bases were œdematous. The heart muscle was pale, and the coronary arteries were slightly atheromatous. There were five pints of clear fluid in the peritoneal cavity.

Liver (weight not recorded). In shape and size this organ was practically normal. It was universally tough and hobnailed. The left lobe contained many circumscribed pale areas. Some of these were hard, and resembled new growth. Others were soft and breaking down; one especially, on the front of the left lobe, contained soft pultaceous material. There was no evidence of hæmorrhage into the breaking-down areas. No growth could be found elsewhere in the body.

Secondary deposits, none.

Histology.—An examination of microscopic slides showed :—

1. Well-marked cirrhotic liver.
2. "Regeneration" nodules, "adenomata" and malignant change.
3. Masses of multinucleated atypical cells.
4. Continuity of growth with liver cells.

Case 6.—Primary carcinoma of liver, with a deposit in dorsal vertebræ. (Dr. Nicholson's slides. Inspection 408, 1903.)

(This is a case of unusual interest, which is described in the post-mortem records as one of sarcoma of the vertebræ.)

Clinical history.—J. E., æt. 67 (optician). Admitted 19th August, 1903, under the care of Dr. Taylor. Died 20th October, 1903. He was admitted into the hospital for paraplegia. For two months before admission he had had pain between the scapulæ. Three weeks before admission the left leg began to get weak, followed a week later by weakness of the right leg. After admission he suffered from incontinence of urine and fæces. He gradually got weaker and died. There were no symptoms recorded suggestive of liver disease. There was no jaundice or ascites. The urine appears to have been darker in colour than normal.

Summary of the autopsy, performed by Dr. Barber.—A soft vascular growth was found between the bodies of the third and fourth dorsal vertebræ, situated chiefly on the left side. There was a constriction of the spinal cord opposite this mass of new growth. The rest of the vertebral column and spinal cord appeared to be normal.

Liver (weight not recorded).—The liver was enlarged. A large round mass of new growth was seen on the upper part of the right lobe, about two inches in diameter.

Histology.—(Specimens of the liver were not kept, and the only available slides are those of Dr. Nicholson's.) The mass in the liver was a primary carcinoma of that organ, and that in the vertebræ was a secondary deposit consisting of typical hepatic cells.

CONCLUSIONS.

1. Primary carcinoma of the liver is extremely rare, being ·1 per cent. of all hospital cases.

2. The post-mortem finding of "no growth elsewhere" is not sufficient to justify a diagnosis of primary carcinoma in the liver. Latent growth in prostate, breasts, or other glandular structures may have given rise to the neoplasm.

3. The disease runs a very rapid course; the average duration of the illness being three and a half months.

4. Cirrhosis is a predisposing cause of primary carcinoma. Four out of the six cases were examples of carcinoma following cirrhosis.

5. The new growth in these cirrhotic cases is due to an attempted regeneration on the part of the liver cells which, in the absence of a controlling influence, follow the course of malignant disease.

6. The cells of the new growth in some instances tend to simulate the arrangement of other glandular structures, *e.g.*, pancreas and suprarenal.

7. Bile occurs in the neoplasm in a few cases.

APPENDIX.

Analysis of 144 Cases of Secondary Carcinoma of the Liver collected from post-mortem reports of Guy's Hospital for ten years (1897–1906 inclusive).

Seat of primary growth.	Number of cases of secondary carcinoma in the liver.	Sex.		Total number of cases of carcinoma during same period.	Percentage of cases giving secondary deposits in liver.
		Male.	Female.		
Stomach	29	16	13	121	35·09
Œsophagus	17	13	4	79	21·5
Rectum	15	9	6	54	27·7
Colon	10	5	5	34	29·4
Sigmoid Flexure ...	11	8	3	35	31·4
Duodenum	5	3	2	8	62·5
Cæcum	2	1	1	10	20·0
Ileum	1	—	1	4	25·0
Pharynx	1	1	—	7	14·2
Gall bladder	12	—	12	22	58·3
Bile ducts	2	1	1	2	
Pancreas	13	7	6	29	44·8
Kidney	3	3	—	10	30·0
Prostate	3	3	—	6	50·0
Bronchus	3	3	—	11	27·3
Lung	1	—	1	4	25·0
Tongue	1	1	—	24	4·2
Lip	1	1	—	3	33·3
Testicle	1	1	—	2	50·0
Carcinoma of many organs (? origin) ...	1	1	—	—	—
Mammary gland (female)	5	—	5	21	23·8
Ovary	4	—	4	14	38·6
Uterus	3	—	3	19	15·8
Bladder	—	—	—	6	—
Larynx	—	—	—	6	—
Floor of mouth ...	—	—	—	3	—
Peritoneum and omentum	—	—	—	3	—
Suprarenal	—	—	—	2	—
Anus	—	—	—	2	—
Penis	—	—	—	2	—
Vulva	—	—	—	2	—
Tonsil	—	—	—	2	—
Scrotum	—	—	—	1	—
Antrum, Highmore's	—	—	—	1	—
	144	77	67	549	—

All figures and statistics are more or less fallacious, and convey only a rough idea of the prevalence, mortality, etc., of malignant

disease. Figures obtained from a general hospital are certain to differ from those obtained from special hospitals. A comparison of some of the results obtained in the above table with those obtained by the Cancer Research Laboratories of the Middlesex Hospital is interesting. While our figures only include cases for a period of ten years, their record is of cases for forty-six years.[1]

The following is a comparison of the percentages of metastatic deposits in the liver from carcinoma in other organs.

	Guy's Hospital.	Middlesex Hospital.
Stomach ...	35·09 ...	39·0
Œsophagus ...	21·5 ...	31·0
Rectum ...	27·7 ...	40·0
Colon ...	29·4 ...	26 0
Prostate ...	50·0 ...	43·0
Bladder ...	None. ...	9·0
Breast ...	23.8 ...	47·0
Ovaries ...	38·6 ...	24·5
Uterus ...	15·8 ...	11·9

A point of interest here is the large proportion of secondary deposits given by the prostate as compared with those given by the bladder. There were six cases of carcinoma of the bladder in our series, of which none gave metastases. In the figures of the Middlesex Hospital there were thirty cases, and in only three instances were deposits found in the liver. The explanation possibly is that the liver is not a suitable place for bladder tissue to grow.

In conclusion, I wish to express my thanks to the physicians of Guy's Hospital for kindly allowing me to make use of the cases recorded in this paper; also to Dr. Fawcett for permission to examine the specimens in the Curator's Room of the Museum, and to Dr. Boycott and Dr. Nicholson for their kind assistance.

REFERENCES.

1. Rolleston, H. D.—Diseases of the liver and bile ducts. London, 1905.
2. Osler, W.—Principles and practice of medicine. London, 1906.

3. Williams, W. Roger.—The Lancet, London, vol. i., 1897, p. 1328. The malignant tumours of infancy, childhood and youth.
4. Miller, C. H. and Cleland, T. B.—Arch. of the Path. Inst. of the London Hosp. London, vol. i., 1906, p. 5. Two cases of primary carcinoma of the liver in infants.
5. Murchison, Chas.—Clinical lectures on diseases of the liver. London, 1885. Lect. vi., p. 261.
6. Taylor, Frederick.—The Clin. Journ., London, 1907, vol. xxx., p. 49. Some unusual forms of pyrexia.
7. Mellanby, Edwd.—Journ. of Phys., London, vol. xxxvi., 1907–8, p. 447. Creatin and Creatinin.
8. Muir, Robt.—Journ. of Path. and Bac., Cambridge, vol. xii., 1908, p. 286. On proliferation of the cells of the liver.
9. Turnbull, H. M., and Worthington, R.—Arch. of Path. Inst. of the London Hosp., London, vol. ii., 1908, p. 59. Three cases illustrating the transition from regeneration to carcinoma in cirrhosis of the liver.
10. Colwell, H.—Arch. of the Middlesex Hosp., London, vol. v., 1905, p. 123. Malignant disease of the liver and bile passages: A statistical study of the records of the Middlesex Hospital.